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Separate and combined associations of obesity and metabolic health with coronary heart disease: a pan-European case-cohort analysis

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Separate and combined associations of obesity and metabolic health with coronary heart disease: a pan-European case-cohort analysis

Table S1. Baseline characteristics [a] and metabolic health status in members of the subcohort, by country

	Denmark	Greece	Germany	Italy	Netherlands	Spain	Sweden	United Kingdom
N	1895	1124	1356	1800	1270	550	1481	998
Age (years)	56.6 (4.4)	52.2 (12.2)	50 (8.7)	50.3 (7.9)	52.7 (10.7)	50.6 (8.4)	57.6 (7.7)	57 (10.7)
Women (%)	46.7	61.7	60.5	66.3	83.9	68.0	61.7	60.6
MetS (%)	27.3	28.1	29.3	22.1	24.1	26.6	25.7	22.1
Normal weight (%)	43.8	27.9	45.6	45.7	51.8	23.3	51.7	51.5
Overweight (%)	42.6	42.0	39.3	39.4	36.4	46.9	37.0	37.5
Obese (%)	13.7	30.1	15.1	14.8	11.8	29.8	11.3	11.0
MHO (% of the obese)	38.6	55.0	31.7	46.8	48.7	57.9	37.1	40.9

[a] Values are unadjusted means (SD) or percentages.

n= 10,474 members of the subcohort included in the analytical sample

Abbreviations: MHO, metabolically healthy obese; MetS, metabolic syndrome

Table S2. Sensitivity analysis: HR for CHD in different complete-case samples specific to each analysis.

		HR [a]	95% CI	p	N cases	N total	I^{2} [b]	95% CI
BMI and Waist Circumference								
Model 1 [c]								
BMI		1.24	(1.17, 1.30)	<.0001	9212	23634	55%	(6%, 79%)
Waist circumference		1.31	(1.24, 1.38)	<.0001	9212	23634	47%	(0%, 76%)
Model 2 [d]								
BMI		1.05	(0.97, 1.14)	0.23	9212	23634	33%	(0%, 69%)
Waist circumference		1.24	(1.12, 1.37)	<.0001	9212	23634	40%	(0%, 73%)
Model 3 [e]								
BMI		1.06	(1.01, 1.10)	0.01	8319	18700	6%	(0%, 68%)
Waist circumference		1.07	(1.01, 1.14)	0.01	8319	18700	21%	(0%, 63%)
Metabolically-defined body size phenotypes								
Model B [f]								
BMI	MetS							
Normal weight	Metabolically Healthy	1.00	(ref)		2833	7664		
Overweight	Metabolically Healthy	1.26	(1.15, 1.38)	<.0001	2513	6748	0%	(0%, 68%)
Obese	Metabolically Healthy	1.41	(1.15, 1.72)	<.0001	687	2159	47%	(0%, 77%)
Normal weight	Metabolically Unhealthy	1.98	(1.67, 2.35)	<.0001	530	929	0%	(0%, 68%)
Overweight	Metabolically Unhealthy	2.26	(1.90, 2.67)	<.0001	2172	3703	63%	(19%, 83%)
Obese	Metabolically Unhealthy	2.44	(2.11, 2.82)	<.0001	1356	2495	4%	(0%, 69%)

[a] Country-specific HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. HRs were combined by multivariate random-effect meta-analysis across 8 countries. Age was used as the underlying time scale, models were stratified by sex and centre.

[b] Heterogeneity across 8 European countries.

[c] Model 1. HRs adjusted for age, smoking, physical activity, Mediterranean diet score, energy and alcohol intake, educational level

[d] Model 2. Model 1 + waist circumference (for BMI) or BMI (for waist circumference)

[e] Model 3. HRs adjusted for age, smoking, systolic blood pressure, total cholesterol, HDL cholesterol, history of diabetes

[f] Model B. HRs adjusted for age, smoking, educational level, physical activity, Mediterranean diet score, energy and alcohol intake

Table S3. Sensitivity analysis: HR for CHD where missing values are imputed by multiple imputation

		HR [a]	95% CI	p
BMI and Waist Circumference				
Model 1 [b]				
BMI		1.28	(1.24, 1.33)	<.0001
Waist circumference		1.32	(1.27, 1.39)	<.0001
Model 2 [c]				
BMI		1.16	(1.07, 1.24)	<.0001
Waist circumference		1.15	(1.05, 1.25)	0.002
Model 3 [d]				
BMI		1.11	(1.06, 1.16)	<.0001
Waist circumference		1.10	(1.04, 1.16)	<.0001
Metabolically-defined body size phenotypes				
Model B [e]				
BMI	MetS			
Normal weight	Metabolically Healthy	1.00	(ref)	
Overweight	Metabolically Healthy	1.35	(1.20, 1.52)	<.0001
Obese	Metabolically Healthy	1.67	(1.39, 1.99)	<.0001
Normal weight	Metabolically Unhealthy	1.78	(1.46, 2.18)	<.0001
Overweight	Metabolically Unhealthy	2.22	(1.98, 2.49)	<.0001
Obese	Metabolically Unhealthy	2.43	(2.09, 2.81)	<.0001

[a] HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. Age was used as the underlying time scale, models were stratified by sex and centre. N=25,653 (12,240 cases). 5 imputed datasets, results combined by Rubin's rules.

[b] Model 1. HRs adjusted for age, smoking, physical activity, Mediterranean diet score, energy and alcohol intake, educational level

[c] Model 2. Model 1 + waist circumference (for BMI) or BMI (for waist circumference)

[d] Model 3. HRs adjusted for age, smoking, systolic blood pressure, total cholesterol, HDL cholesterol, history of diabetes

[e] Model B. HRs adjusted for age, smoking, physical activity, Mediterranean diet score, energy and alcohol intake, educational level

Table S4. Sensitivity analysis: HR for CHD after exclusion of first two years of follow-up across metabolically-defined body size phenotypes

BMI	MetS	HR [a]	95%CI	p-value	N cases	N total	I^{2} [b]	95% CI
Model A [c]								
Normal weight	Metabolically Healthy	1.00	(ref)		1802	5961		
Overweight	Metabolically Healthy	1.22	(1.10, 1.35)	<.0001	1581	4241	0%	(0%, 68%)
Obese	Metabolically Healthy	1.24	(0.99, 1.57)	0.07	323	1059	37%	(0%, 72%)
Normal weight	Metabolically Unhealthy	2.12	(1.74, 2.58)	<.0001	428	778	0%	(0%, 68%)
Overweight	Metabolically Unhealthy	2.30	(1.96, 2.72)	<.0001	1678	2946	50%	(0%, 78%)
Obese	Metabolically Unhealthy	2.54	(2.23, 2.91)	<.0001	976	1829	0%	(0%, 68%)
Model B [d]								
Normal weight	Metabolically Healthy	1.00	(ref)		1802	5961		
Overweight	Metabolically Healthy	1.23	(1.11, 1.37)	<.0001	1581	4241	0%	(0%, 68%)
Obese	Metabolically Healthy	1.25	(0.99, 1.58)	0.06	323	1059	35%	(0%, 71%)
Normal weight	Metabolically Unhealthy	2.09	(1.72, 2.54)	<.0001	428	778	0%	(0%, 68%)
Overweight	Metabolically Unhealthy	2.29	(1.90, 2.75)	<.0001	1678	2946	58%	(7%, 81%)
Obese	Metabolically Unhealthy	2.46	(2.14, 2.82)	<.0001	976	1829	0%	(0%, 68%)

[a] Country-specific HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. HRs were combined by multivariate random-effects meta-analysis across 8 countries. Age was used as the underlying time scale, models were stratified by sex and centre. n=16,814 (6,788 CHD cases).
[b] Heterogeneity across 8 European countries
[c] Model A. HRs adjusted for age, smoking, educational level.
[d] Model B included the same variables as model A + physical activity, Mediterranean diet score, energy and alcohol intake

Table S5. Sensitivity analysis: HR for hard CHD (myocardial infarction) across metabolically-defined body size phenotypes

BMI	MetS	HR [a]	95%CI	p-value	N cases	N total	I^2 [b]	95% CI
Model A[c]								
Normal weight	Metabolically Healthy	1.00	(ref)		1303	6165		
Overweight	Metabolically Healthy	1.23	(1.07, 1.41)	0.003	1144	4451	0%	(0%, 68%)
Obese	Metabolically Healthy	1.32	(1.01, 1.73)	0.045	234	1103	43%	(0%, 75%)
Normal weight	Metabolically Unhealthy	2.13	(1.70, 2.67)	<.0001	325	842	12%	(0%, 71%)
Overweight	Metabolically Unhealthy	2.21	(1.92, 2.55)	<.0001	1283	3200	19%	(0%, 62%)
Obese	Metabolically Unhealthy	2.57	(2.17, 3.04)	<.0001	773	1972	12%	(0%, 72%)
Model B [d]								
Normal weight	Metabolically Healthy	1.00	(ref)		1303	6165		
Overweight	Metabolically Healthy	1.24	(1.08, 1.43)	0.002	1144	4451	3%	(0%, 69%)
Obese	Metabolically Healthy	1.30	(1.00, 1.70)	0.049	234	1103	39%	(0%, 73%)
Normal weight	Metabolically Unhealthy	2.10	(1.71, 2.58)	<.0001	325	842	0%	(0%, 68%)
Overweight	Metabolically Unhealthy	2.21	(1.89, 2.57)	<.0001	1283	3200	26%	(0%, 67%)
Obese	Metabolically Unhealthy	2.46	(2.10, 2.90)	<.0001	773	1972	1%	(0%, 68%)

[a] Country-specific HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. HRs were combined by multivariate random-effects meta-analysis across 8 countries. Age was used as the underlying time scale, models were stratified by sex and centre. n=17,733 participants (5,062 CHD cases)
[b] Heterogeneity across 8 European countries
[c] Model A. HRs adjusted for age, smoking, educational level.
[d] Model B included the same variables as model A + physical activity, Mediterranean diet score, energy and alcohol intake

Table S6. Sensitivity analysis: HR for CHD events across metabolically-defined body size phenotypes in non-smokers only

BMI	MetS	HR [a]	95%CI	p-value	N cases	N total	I^{2} [b]	95% CI
Model A [c]								
Normal weight	Metabolically Healthy	1.00	(ref)		1193	4166		
Overweight	Metabolically Healthy	1.22	(1.04, 1.38)	0.003	1173	3215	0%	(0%,68%)
Obese	Metabolically Healthy	1.26	(0.96, 1.67)	0.10	272	871	45%	(0%,76%)
Normal weight	Metabolically Unhealthy	2.15	(1.72, 2.69)	<.0001	277	506	0%	(0%,68%)
Overweight	Metabolically Unhealthy	2.32	(2.00, 2.70)	<.0001	1233	2193	7%	(0%,70%)
Obese	Metabolically Unhealthy	2.59	(2.21, 3.03)	<.0001	763	1443	0%	(0%,68%)
Model B[d]								
Normal weight	Metabolically Healthy	1.00	(ref)		1193	4166		
Overweight	Metabolically Healthy	1.23	(1.08,1.40)	0.002	1173	3215	47%	(0%, 80%)
Obese	Metabolically Healthy	1.29	(0.99,1.67)	0.06	272	871	0%	(0%, 79%)
Normal weight	Metabolically Unhealthy	2.15	(1.71,2.71)	<.0001	277	506	35%	(0%, 75%)
Overweight	Metabolically Unhealthy	2.32	(1.97,2.73)	<.0001	1233	2193	44%	(0%, 80%)
Obese	Metabolically Unhealthy	2.58	(2.18,3.04)	<.0001	763	1443	0%	(0%, 79%)

[a] Country-specific HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. HRs were combined by multivariate random-effects meta-analysis across 8 countries. Age was used as the underlying time scale, models were stratified by sex and centre. n=12,394 (4,911 cases)

[b] Heterogeneity across 8 European countries

[c] Model A. HRs age, smoking (never, former), educational level.

[d] Model B included the same variables as model A + physical activity, Mediterranean diet score, energy and alcohol intake

Table S7. Sensitivity analysis: HR for CHD events with the highest level of certainty across metabolically-defined body size phenotypes

BMI	MetS	HR [a]	95%CI	p-value	N cases	N total	I^2 [b]	95% CI
Model A [c]								
Normal weight	Metabolically Healthy	1.00	(ref)		268	3159		
Overweight	Metabolically Healthy	1.39	(1.04, 1.86)	0.03	325	2598	40%	(0%, 78%)
Obese	Metabolically Healthy	1.11	(0.79, 1.55)	0.55	65	738	0%	(0%, 79%)
Normal weight	Metabolically Unhealthy	2.58	(1.68, 3.95)	<.0001	75	374	21%	(0%, 66%)
Overweight	Metabolically Unhealthy	2.78	(2.17, 3.57)	<.0001	389	1707	3%	(0%, 80%)
Obese	Metabolically Unhealthy	2.99	(2.36, 3.79)	<.0001	262	1218	0%	(0%, 79%)
Model B[d]								
Normal weight	Metabolically Healthy	1.00	(ref)		268	3159		
Overweight	Metabolically Healthy	1.44	(1.05, 1.99)	0.03	325	2598	47%	(0%, 80%)
Obese	Metabolically Healthy	1.13	(0.81, 1.59)	0.47	65	738	0%	(0%, 79%)
Normal weight	Metabolically Unhealthy	2.79	(1.73, 4.49)	<.0001	75	374	35%	(0%, 75%)
Overweight	Metabolically Unhealthy	2.88	(2.09, 3.98)	<.0001	389	1707	44%	(0%, 80%)
Obese	Metabolically Unhealthy	2.93	(2.29, 3.77)	<.0001	262	1218	0%	(0%, 79%)

[a] Country-specific HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. HRs were combined by multivariate random-effects meta-analysis across 8 countries. Age was used as the underlying time scale, models were stratified by sex and centre. n=9,794 (1,384 cases)

[b] Heterogeneity across 8 European countries

[c] Model A. HRs adjusted for age, smoking, educational level.

[d] Model B included the same variables as model A + physical activity, Mediterranean diet score, energy and alcohol intake

Table S8. Sensitivity analysis: HR for CHD across metabolically-defined body size phenotypes separately for men and women

BMI	MetS	HR [a]	95%CI	p-value	N cases	N total	I^{2} [b]	95% CI
Men								
Normal weight	Metabolically Healthy	1.00	(ref)		1053	2310		
Overweight	Metabolically Healthy	1.32	(1.16, 1.51)	<.0001	1168	2328	0%	(0%,68%)
Obese	Metabolically Healthy	1.28	(0.99, 1.65)	0.06	184	415	7%	(0%,70%)
Normal weight	Metabolically Unhealthy	2.53	(1.90, 3.37)	<.0001	243	346	45%	(0%,76%)
Overweight	Metabolically Unhealthy	2.35	(2.03, 2.73)	<.0001	1239	1861	25%	(0%,66%)
Obese	Metabolically Unhealthy	2.47	(2.06, 2.95)	<.0001	622	954	0%	(0%,68%)
Women								
Normal weight	Metabolically Healthy	1.00	(ref)		925	3855		
Overweight	Metabolically Healthy	1.19	(1.03, 1.38)	0.02	609	2123	0%	(0%,68%)
Obese	Metabolically Healthy	1.28	(1.02, 1.60)	0.03	176	688	0%	(0%,68%)
Normal weight	Metabolically Unhealthy	1.85	(1.48, 2.31)	<.0001	248	496	0%	(0%,68%)
Overweight	Metabolically Unhealthy	2.36	(2.01, 2.76)	<.0001	677	1339	26%	(0%,67%)
Obese	Metabolically Unhealthy	2.72	(2.27, 3.26)	<.0001	493	1018	30%	(0%,69%)

[a] Country-specific HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. HRs were combined by multivariate random-effects meta-analysis across 8 countries. Age was used as the underlying time scale, models were stratified by sex and centre. n=8,214 men (4,509 cases) and n=9,519 (n=3,128 cases).
HRs adjusted for age, smoking (never, former), educational level, physical activity, Mediterranean diet score, energy and alcohol intake
[b] Heterogeneity across 8 European countries

Table S9. Sensitivity analysis: HR for CHD in metabolically-defined body size phenotypes where the definition of MetS does not include the waist circumference criterion

BMI	MetS without WC	HR [a]	95%CI	p-value	N cases	N total	I^2 [b]	95% CI
Model A [c]								
Normal weight	Metabolically Healthy	1.00	(ref)		1458	5166		
Overweight	Metabolically Healthy	1.36	(1.20, 1.56)	<.0001	1532	3999	6%	(0%, 69%)
Obese	Metabolically Healthy	1.43	(1.13, 1.81)	0.003	357	1095	42%	(0%, 74%)
Normal weight	Metabolically Unhealthy	2.01	(1.72, 2.35)	<.0001	1011	1841	19%	(0%, 62%)
Overweight	Metabolically Unhealthy	2.52	(2.17, 2.94)	<.0001	2161	3652	41%	(0%, 74%)
Obese	Metabolically Unhealthy	2.92	(2.54, 3.34)	<.0001	1118	1980	0%	(0%, 68%)
Model B [d]								
Normal weight	Metabolically Healthy	1.00	(ref)		1458	5166		
Overweight	Metabolically Healthy	1.38	(1.20, 1.57)	<.0001	1532	3999	7%	(0%, 70%)
Obese	Metabolically Healthy	1.43	(1.14, 1.81)	0.002	357	1095	39%	(0%, 73%)
Normal weight	Metabolically Unhealthy	2.00	(1.72, 2.32)	<.0001	1011	1841	8%	(0%, 70%)
Overweight	Metabolically Unhealthy	2.49	(2.11, 2.94)	<.0001	2161	3652	48%	(0%, 77%)
Obese	Metabolically Unhealthy	2.82	(2.45, 3.25)	<.0001	1118	1980	0%	(0%, 68%)

[a] Country-specific HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. HRs were combined by multivariate random-effect meta-analysis across 8 countries. Age was used as the underlying time scale, models were stratified by sex and centre. n=17,733 participants (7,637 CHD cases)

[b] Heterogeneity across 8 European countries

[c] Model A. HRs adjusted for age, smoking, educational level.

[d] Model B included the same variables as model A + physical activity, Mediterranean diet score, energy and alcohol intake

Table S10. Sensitivity analysis: HR for CHD in metabolically-defined body size phenotypes where "metabolically healthy" is defined as having none of the 4 abnormalities

BMI	Healthy defined as having 0 abnormality	HR [a]	95%CI	p-value	N cases	N total	I^{2} [b]	95% CI
Model A [c]								
Normal weight	Metabolically Healthy	1.00	(ref)		390	2148		
Overweight	Metabolically Healthy	1.24	(0.99, 1.56)	0.06	260	1040	0%	(0%, 68%)
Obese	Metabolically Healthy	1.15	(0.72, 1.84)	0.55	36	198	0%	(0%, 68%)
Normal weight	Metabolically Unhealthy	1.93	(1.62, 2.31)	<.0001	2079	4859	0%	(0%, 68%)
Overweight	Metabolically Unhealthy	2.67	(2.29, 3.12)	<.0001	3433	6611	0%	(0%, 68%)
Obese	Metabolically Unhealthy	3.19	(2.64, 3.85)	<.0001	1439	2877	0%	(0%, 68%)
Model B [d]								
Normal weight	Metabolically healthy	1.00	(ref)		390	2148		
Overweight	Metabolically Healthy	1.24	(0.99, 1.56)	0.06	260	1040	0%	(0%, 68%)
Obese	Metabolically Healthy	1.21	(0.76, 1.92)	0.43	36	198	0%	(0%, 68%)
Normal weight	Metabolically Unhealthy	1.94	(1.62, 2.32)	<.0001	2079	4859	0%	(0%, 68%)
Overweight	Metabolically Unhealthy	2.68	(2.28, 3.14)	<.0001	3433	6611	0%	(0%, 68%)
Obese	Metabolically Unhealthy	3.12	(2.57, 3.80)	<.0001	1439	2877	2%	(0%, 68%)

[a] Country-specific HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. HRs were combined by multivariate random-effects meta-analysis across 8 countries. Age was used as the underlying time scale, models were stratified by sex and centre. n=17,733 participants (7,637 CHD cases)
[b] Heterogeneity across 8 European countries
[c] Model A. HRs adjusted for age, smoking, educational level.
[d] Model B included the same variables as model A + physical activity, Mediterranean diet score, energy and alcohol intake

Table S11. Sensitivity analysis: HR for CHD in metabolically-defined body size phenotypes where obesity is defined by WC, and MetS does not include criteria on WC

WC	MetS without WC	HR [a]	95%CI	p-value	N cases	N total	I^2 [b]	95% CI
Model A [c]								
Normal WC [d]	Metabolically Healthy	1.00	(ref)		1653	5707		
Overweight [e]	Metabolically Healthy	1.40	(1.15, 1.69)	0.001	1031	2729	55%	(0%, 80%)
Obese [f]	Metabolically Healthy	1.37	(1.11, 1.69)	0.003	663	1824	50%	(0%, 78%)
Normal WC [d]	Metabolically Unhealthy	1.96	(1.70, 2.25)	<.0001	1143	2075	0%	(0%, 68%)
Overweight [e]	Metabolically Unhealthy	2.43	(2.09, 2.82)	<.0001	1340	2292	20%	(0%, 62%)
Obese [f]	Metabolically Unhealthy	2.92	(2.47, 3.45)	<.0001	1807	3106	47%	(0%, 76%)
Model B [g]								
Normal WC [d]	Metabolically Healthy	1.00	(ref)		1653	5707		
Overweight [e]	Metabolically Healthy	1.41	(1.17, 1.70)	<.0001	1031	2729	53%	(0%, 79%)
Obese [f]	Metabolically Healthy	1.39	(1.12, 1.73)	0.003	663	1824	51%	(0%, 78%)
Normal WC [d]	Metabolically Unhealthy	1.94	(1.68, 2.24)	<.0001	1143	2075	0%	(0%, 68%)
Overweight [e]	Metabolically Unhealthy	2.43	(2.09, 2.84)	<.0001	1340	2292	24%	(0%, 65%)
Obese [f]	Metabolically Unhealthy	2.84	(2.38, 3.39)	<.0001	1807	3106	50%	(0%, 77%)
Model C [h]								
Normal WC [d]	Metabolically Healthy	1.00	(ref)		1653	5707		
Overweight [e]	Metabolically Healthy	1.33	(1.10, 1.60)	<.0001	1031	2729	44%	(0%, 75%)
Obese [f]	Metabolically Healthy	1.22	(0.99, 1.51)	0.06	663	1824	25%	(0%, 66%)
Normal WC [d]	Metabolically Unhealthy	1.93	(1.66, 2.24)	<.0001	1143	2075	0%	(0%, 68%)
Overweight [e]	Metabolically Unhealthy	2.26	(1.92, 2.66)	<.0001	1340	2292	21%	(0%, 63%)
Obese [f]	Metabolically Unhealthy	2.44	(1.99, 2.99)	<.0001	1807	3106	25%	(0%, 66%)

[a] Country-specific HRs were estimated from Prentice-weighted Cox proportional hazards models, and 95%CI estimated with robust variance, to take into account the case-cohort design. HRs were combined by multivariate random-effect meta-analysis across 8 countries. Age was used as the underlying time scale, models were stratified by sex and EPIC study centre. n=17,733 participants (7,637 CHD cases); [b] Heterogeneity across 8 countries;
[c] Model A. HRs adjusted for age, smoking, educational level.;
[d] Normal WC: WC<94 for men, 80 for women; [e] Overweight: 94≤WC<102 for men, 80≤WC<88 for women; [f] Obese: WC≥102 for men, 88 for women
[g] Model B included the same variables as model A + physical activity, Mediterranean diet score, energy and alcohol intake
[h] Model C included the same variables as model B + BMI

Table S12. Cross-classification in metabolically-defined body size phenotypes where body size is defined by BMI or by WC

BMI-defined	WC-defined						
	MHANW	MUANW	MHAOW	MUAOW	MHAO	MUAO	Total
MHNW	4447	999	648	0	71	0	6165
MUNW	0	394	0	391	0	57	842
MHOW	1246	452	1905	0	848	0	4451
MUOW	0	218	0	1753	0	1229	3200
MHO	14	8	176	0	905	0	1103
MUO	0	4	0	148	0	1820	1972
Total	5707	2075	2729	2292	1824	3106	17733

Abbreviations: MHNW, metabolically healthy normal weight; MUNW, metabolically unhealthy normal weight; MHOW, metabolically healthy overweight; MUOW, metabolically unhealthy overweight; MHO, metabolically healthy obese; MUO, metabolically unhealthy obese; MHANW, metabolically healthy abdominally normal weight; MUANW, metabolically unhealthy abdominally normal weight; MHAOW, metabolically healthy abdominally overweight; MUAOW, metabolically unhealthy abdominally overweight; MHAO, metabolically healthy abdominally obese; MUAO, metabolically unhealthy abdominally obese.

Weighted kappa (95%CI), measuring agreement between two classifications, was 0.667 (0.660- 0.674)

Figure S1. Schematic representation of the EPIC-CVD case-cohort design and sample included in the complete-case analysis

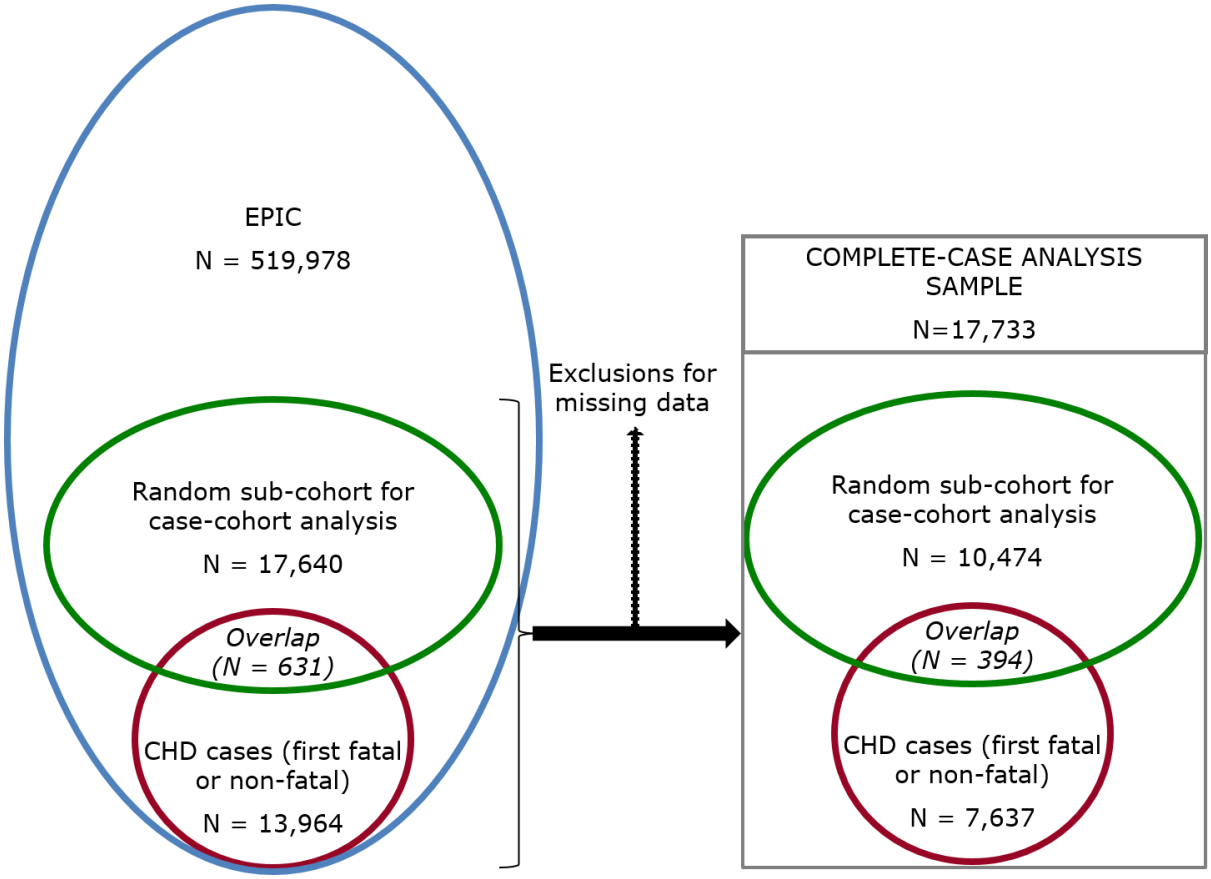


Figure S2. Schematic representation of the analysis strategy

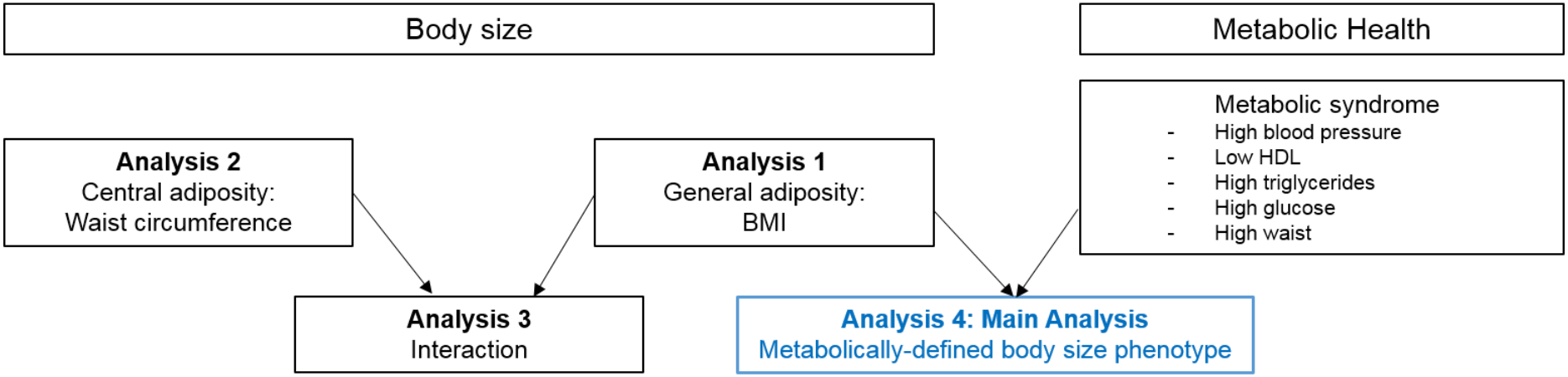
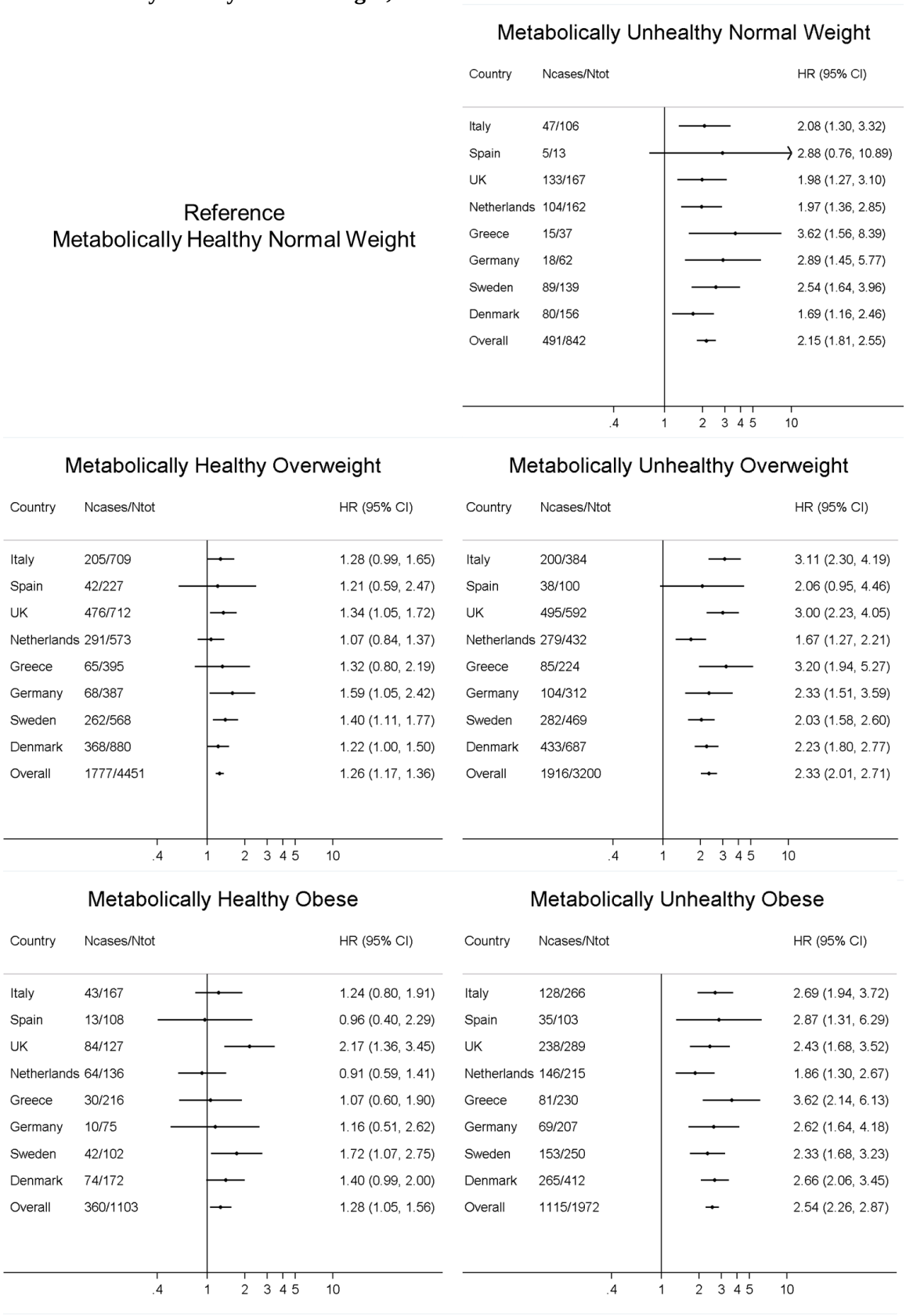


Figure S3. Country-specific HRs across metabolically-defined body size phenotypes compared to metabolically healthy normal weight, Model B [a]



[a] Model B was adjusted for age, smoking, educational level, physical activity, Mediterranean diet score, energy and alcohol intake